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PREPARATION AND EVALUATION OF A SYSTEM FOR EXPOSING RATS TO TOLUENE DIISOCYANATE VAPOUR

Report for

The International Isocyanate Institute

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CONTENTS

1. SUMMARY

1. A laboratory system has been developed for the generation and analysis of toluene diisocyanate (TDI) vapour.

2. Using this system the Marcali spectrophotometric analytical method and the Model 7000 monitor for estimation of TDI vapour concentrations have been compared and give good agreement.

3. A facility has been prepared for exposing rats to TDI vapour. TDI atmospheres in inhalation chamber have been generated to the required concentrations (0.05 and 0.15 ppm).

4. Good control of temperature and humidity has been achieved in these chambers.

5. When TDI vapour is transferred to the chambers a good distribution is achieved in the upper part of the chamber. As the vapour passes to the lower part some loss of TDI occurs. Typically, if the mean concentration in the chamber is 0.042 ppm, the mean concentration at the top is 0.051 ppm and at the bottom 0.035 ppm. The loss is probably due to the combined effects of hydrolysis and surface adsorption in the chamber. A similar effect occurs at 0.15 ppm. During the inhalation study, rat cage positions will be changed regularly to minimise this problem.

6. Lateral distribution of TDI vapour in the chamber is good.

7. A dilution system has been developed for use with the TDI monitor, for analysis of TDI vapour at the higher concentration (0.15 ppm).

8. The Marcali method and the TDI monitor give comparable TDI levels in the inhalation chambers, with and without the use of the monitor dilution equipment.

2. INTRODUCTION

An investigation has been initiated into the effects of toluene diisocyanate (TDI) vapour on rats and golden hamsters exposed over an 18 month period.

For all inhalation studies the control of exposure conditions is important, particularly the concentration and distribution of test material in the exposure chamber. This applies especially to studies with TDI because the chemical and physical characteristics of the compound make control of atmospheres at low concentrations potentially difficult, i.e., the compound is readily hydrolysed in moist air and also adsorbed onto surfaces.

As a first step towards development of suitable exposure conditions a system was prepared on the laboratory scale for generation of stable TDI atmospheres by passing dry air through TDI liquid maintained at a constant temperature. Two analytical methods have been used and compared for monitoring these atmospheres - the spectrophotometric method of Marcali (1957) and the Model 7000 TDI Monitor.

A similar system was then developed for generation of TDI atmospheres in large inhalation chambers and for monitoring the distribution of TDI within the chambers.

This report describes the systems developed and the results obtained with them.

3. EXPOSURE SYSTEM

3.1 Room design

The room prepared for rat exposure in this study is L-shaped. The main area measures 5.2 x 6.6 metres and the additional area is 2.6 x 2.6 metres (Fig.1). The room is constructed of brick and composition brick with a concrete roof and suspended false ceiling.

Two inhalation chambers stand against one wall of the room and a third occupies the recess in the opposite wall. A false floor has been built over the rest of the room at the level of the bottom of the chambers (0.5 m high) to allow easy access with batteries and generation equipment. This floor is finished with a polyvinyl material.

An automatic lift in one corner of the room is used to raise batteries to the false floor.

The room air is temperature and humidity controlled (22 $\pm$ 2°C, 50 $\pm$ 5%) and filtered before entering the room.

The room windows are covered in a translucent plastic material principally for security purposes, but also to diffuse direct sunlight.

3.2 Inhalation chambers

Three inhalation chambers have been prepared for rat exposures in this study. These are essentially cubic (external dimensions 2.1m x 2.1m x 2.1m) with a pyramidal top (28 cm vertical height) and a base sloping 12 cm towards one rear corner. The chambers have a stainless steel framework and three stainless steel sides.

The two doors on one side are of laminated glass in a stainless steel frame and open on vertical hinges at the side of the chamber. They are carefully sealed to prevent leaks with a silicone rubber strip which is stuck to the frame with cyanoacrylic adhesive. This is preferred to other rubbers because of reduced cross linking in the presence of TDI.

The main air flow into the chambers is drawn from the room through a 22 cm filter. The flow rate is displayed on a Model IGU/2B flowmeter (Paton Flow Control Ltd., Basingstoke) and the air enters the top of the chamber through a stainless steel head at a tangential angle to encourage distribution of TDI in the inhalation chamber. The chambers are operated at negative pressure, air being withdrawn from the centre of the bottom plate, with a fan-filter unit (Microflow Ltd., Portsmouth). Each chamber has a water manometer to indicate the effectiveness of the door seal. Measurements in the closed chambers show a pressure reduction of 14 mm water at a flow rate of 1.0 cu.metre/minute. Each chamber has a 3.5 cm diameter drain at the lowest

point in the chamber for cleaning purposes.

Nine sampling points are available in each chamber.

Each chamber has two sets of adjustable runners for easy loading and unloading of cage batteries directly from the false floor. The batteries each hold 20 galvanised wire mesh cages (Associated Crates Ltd., Stockport). These cages measure 55 x 31 x 20 cm and will readily accommodate 6 rats each. They are equipped with food hoppers and water bottles which are easily removed for the exposure period. Excreta is collected on paper-covered galvanised trays.

Each inhalation chamber is equipped with a maximum and minimum thermometer and chamber temperatures will be monitored daily. Chamber humidity will be monitored at regular intervals during each day using a hair hygrometer. This will be checked with a psychrometer at monthly intervals. If TDI vapour has a deleterious effect on these instruments, measurements will be made only in the control rat chamber.

3.3 Generation system

The generation and transfer of TDI to the inhalation chambers takes place in an all-glass system. TDI is generated by bubbling dry air through the liquid held in a Dreschel bottle. Compressed air is used as a source and is dried in an automatically rechargeable molecular sieve unit (Autozorber Model AB12.5 - Rimer Berlec Ltd., Cardiff) Two Dreschel bottles are held in a

water bath at 59°C and air is bubbled through at 5.0 l/min (for 0.15 ppm concentration) and 2.2 l/min (for 0.05 ppm). The flow rates are controlled with model GS/$^{1}/_{4}$" B flowmeters (Platon Flow Control Ltd.). The TDI liquid is replaced daily to avoid build-up of hydrolysis products.

The TDI vapour generated is then transferred in approximately 2 or 6 metres of glass pipe (2.5 cm diameter) to the head of the inhalation chamber, where it is mixed with air at 1000 l/min before passing into the chamber. All junctions in glass piping employ spherical joints (S 41). A similar joint of stainless steel is incorporated into the mixing head at the top of the chamber. The generation equipment is held in a ventilated hood adjacent to the chambers. The system is shown schematically in Figs.2 and 3 in Fig. 2A.

3.4 Monitoring system

One Model 7000 TDI monitor is used in this study. It is connected to receive sample atmospheres from three areas - the two chambers containing TDI vapour and the room in which the study is conducted. The TDI monitoring system, which is all-glass, is shown in Fig.4. The atmosphere of the room will be analysed without dilution, but the atmosphere from the two inhalation chambers will be diluted with dry air before transfer to the monitor, using the system in Fig.4. The monitor will be switched to each atmosphere in turn for a short period

and the mean concentration obtained recorded on the form shown in Fig. 5, together with other relevant details of chamber atmosphere control. On many occasions, particularly using this monitoring system, losses of TDI vapour were observed in glass tubing, resulting in low yields of TDI. The most satisfactory treatment found to minimise this effect was to treat all glassware with a solution of chromium trioxide in concentrated sulphuric acid for 16 hours at room temperature.

4. LABORATORY STUDIES

The purpose of these studies was twofold. Firstly to develop some experience and expertise in the handling of TDI and the generation and estimation of vapour atmospheres. Secondly to satisfy ourselves that the monitoring techniques available were satisfactory on a small scale before moving to larger scale TDI atmosphere generation.

4.1 Generation of TDI vapour for laboratory studies

4.1.1 Principle

TDI vapour was generated by the passage of dry nitrogen through liquid TDI maintained at a constant temperature. The saturated vapour produced was diluted further with air to produce the required concentrations, in this case approximately 0.01, 0.02, 0.03, 0.04 and 0.05 ppm. The system, which was similar to that used by Miller & Mueller (1975) was used for 2 purposes - checking the spectrophotometric method of analysis for TDI (Marcali, 1957) and checking the calibration of the Model 7000 TDI monitor.

4.1.2 Method

The apparatus used is shown schematically in Fig.6 & 6A. The TDI liquid was held in a glass Dreschel bottle which was suspended in a water bath at constant temperature (21°). Nitrogen, from a compressed gas cylinder, was dried over molecular sieve and the flow rate adjusted to 40 ml/min. This was then bubbled through the TDI liquid and the resulting vapour was transferred to an all-glass dilution and mixing system. Diluent air at a controlled flow rate (5-20 l/min)

was mixed with the saturated vapour in a glass coil (8 mm i.d., 100 cm long), before transfer to a glass manifold 25 cm long and 2 cm diameter. Vapour was extracted from the manifold in three ways - through a Model 7000 TDI monitor, simultaneously through an absorption trap for spectrophotometric assay and the excess to a safe exhaust.

4.2 Analysis of Toluene Diisocyanate (TDI) in air

4.2.1 Spectrophotometric method (Marcali, 1957)

4.2.1.1 Principle

Marcali (1) has described a method for analysis of TDI in gas atmospheres. TDI is trapped in an acidic absorbent, hydrolysed to the diamine, diazotised and coupled to N - 1 - naphthylethylenediamine. The TDI concentration is then determined by spectrophotometry of the coloured solution. The method does not detect the main hydrolysis products of TDI.

The method has been rewritten for routine use in the laboratory at HLE.

4.2.1.2 Apparatus

Spectrophotometer. Perkin Elmer model 124 double beam spectrophotometer, with 40 mm silica cells. Dreschel bottles with sintered glass tubes, to accommodate 15 ml absorber medium. These bottles are graduated at the 20 ml level.

4.2.1.3 Reagents

Glacial Acetic acid analar - British Drug Houses Ltd. (BDH) Analytical grade

Concentrated hydrochloric acid Analar - BDH. Analytical grade.

Sodium nitrite - BDH Laboratory reagent grade

Sodium bromide - BDH Laboratory reagent grade

Sulphamic acid (dry) - BDH Laboratory reagent grade

N-1-Naphthylethylenediamine dihydrochloride - BDH Laboratory reagent grade

Sodium Nitrite Solution - Dissolve sodium nitrite (3g) and sodium bromide (5g) in water (80 ml) and dilute to 100 ml with water. Prepare fresh daily.

Absorption medium

Add concentrated hydrochloric acid (35 ml) and glacial acetic acid (22 ml) to approximately 600 ml water and dilute to 1 litre. The solution is then approximately 0.4 N with respect to hydrochloric acid and acetic acid.

N-1-Naphthylethlenediamine solution

Dissolve 50 mg in water (25 ml), add conc Hydrochloric acid (1 ml) and dilute to 50 ml, with water. Prepare fresh daily.

Sulphamic acid solution

Prepare a 10% w/v solution of the dry acid in water.

Acetic acid solution (8.8N)

Prepare 8.8N acetic acid by mixing glacial acetic acid (500 ml) with water (approximately 300 ml) and diluting to 1 litre.

Acetic acid (0.6N) solution

Add glacial acetic acid (29 ml) to water and adjust to 1 litre.

Standard Toluene-2-4diisocyanate solutions

Solution A

Carefully weigh approximately 222 mg pure toluene-2,4-diisocyanate into 660 ml glacial acetic acid. Agitate to dissolve the diisocyanate. Immediately dilute to 1 litre with water in a glass-stoppered volumetric flask. This solution should be used within 15 minutes after final dilution to prepare solution B.

Solution B

Transfer an aliquot of solution A (10 ml) to a glass-stoppered 1 litre volumetric flask. Add a 8.8N acetic acid (55 ml) so that when solution B is diluted to 1 litre with water it will be 0.6N with respect to acetic acid. Dilute to 1 litre with water. Use within 15 minutes. 1 ml of solution B contains approximately 0.0022 mg of toluene-2,4-diisocyanate.

4.2.1.4 Procedure

Bubble TDI vapour through absorption medium (15 ml) for a pre-determined time (usually 6 minutes) at a flow rate of 950 ml/min.

Prepare two blank samples by pipetting absorption medium (15 ml) into Dreschel bottles. After trapping TDI vapour add 3% sodium nitrite solution (0.5 ml) to blank and test absorption bottles. Shake the bottles and allow to stand for 90 seconds. Add 10% sulphamic acid solution (1 ml), shake, and allow to stand for 2 minutes to destroy excess nitrous acid. Add 0.1% N-naphthylethylenediamine solution (1 ml), shake and stand for 5 minutes to complete colour development. A red-blue colour indicates the presence of TDI. Add water to adjust the final

volume to 20 ml in each cylinder.

Record the absorbance of the solution at 550 mμ, as in section 3.2.1.6.

4.2.1.5 Calibration

Add 1.2N hydrochloric acid (5 ml) to a series of eight graduated absorption bottles. To each bottle add the following reagents and shake:-

Bottle No.	1	2	3	4	5	6	7	8
0.6N acetic acid (ml)	10.0	9.5	9.0	8.0	7.0	6.0	5.0	0.0
Solution B (ml)	0.0	0.5	1.0	2.0	3.0	4.0	5.0	10.0

Develop the red-blue colour according to the method in section 3.2.1.4 and record the absorbance as in section 4.2.1.6. Prepare a calibration curve by plotting absorbance against the mass of TDI in each sample (Fig.1).

4.2.1.6 Spectrophotometry

Set the wavelength to 550 mμ. Fill 2 silica cells (40 mm) with blank solutions and insert into the 2 light beams. Adjust the photometer to give an absorbance reading of 0.0. Insert the 100% transmission slide into the test beam and adjust the spectrophotometer to give an absorbance reading of 1.0. Insert the 10% transmission slide and adjust to give an absorbance reading of 0.90. Repeat these adjustments until all 3 readings are correct.

Remove one blank cell, clean and refill with solution from the first test bottle. Record the absorbance at 550 mμ. Repeat for each test sample.

4.2.1.7 Calculation

If W is the mass of TDI in μg, trapped in the absorption medium and A is the absorbance reading from this solution.

$$W = 15.09A$$

4.2.2 Model 7000 TDI monitor

Principle

This monitor is based on the analytical method developed by Reilly (1968). TDI vapour is passed through a moving strip of dye-impregnated test paper. When sufficient time has elapsed for the derived colour to develop (approximately 15 mins.), the strip is monitored at a fixed wavelength, using an unexposed portion of tape as a reference. A direct logarithmic readout in ppm TDI ($^{v}/_{v}$) is displayed and recorded.

Preparation

The monitor, Serial No. 1264, was supplied by Universal Environmental Instruments Ltd., Poole. Before use it was checked and adjusted to meet the design specification. In particular the flow rate of TDI vapour entering the monitor was adjusted to 500 ml. To do this the integral flowmeter, monitoring the TDI vapour flow rate after passage through the detector tape, was adjusted to 600 ml/min. Flow rates will be checked regularly throughout the study.

5. EVALUATION OF SYSTEM

5.1 Comparison of two methods of analysis

Using the apparatus described in section 4.1, TDI vapour atmospheres were generated at several concentrations. These atmospheres were analysed simultaneously using the Model 7000 Monitor and the Marcali spectrophotometric method. Six estimations were made. The results are shown in Table 1 and Fig. 8.

Good agreement was obtained between the two methods, although minor differences were seen between results obtained by the two methods. Since it is reasonable to expect both analytical methods at these concentrations to have errors in the range 0-10%, the differences obtained between methods are believed to be within the limit of expected experimental error.

The results obtained were comparable with those of Miller & Mueller (1975), in particular the degree of linearity found in both studies was very similar. One difference observed, however, was that in our studies the Marcali method gave a slightly lower result than the Model 7000 monitor, whereas Miller & Mueller obtained slightly higher results with the Marcali method.

Comparison of the results obtained with those of Nelson and Booth (1975) again showed a similar degree of reproducibility at the higher levels, although the published results were more consistent at levels below 0.01 ppm. The monitor will be

compared with the Marcali method at regular intervals throughout the 18 month exposure period.

Both methods are essentially non-responsive to the expected hydrolysis products of TDI.

5.2 Atmospheres within exposure chambers

All assessments have been made with the rat batteries in the chambers but with no animals in the cages. When the study is underway the measurements will be repeated during animal exposure, in case the presence of animals and the resultant potential increase in humidity, affects the chamber atmosphere.

5.2.1 Temperature and humidity

Temperature and humidity within the inhalation chambers is controlled at 22 $\pm$ 2°C and 50 $\pm$ 5% humidity. Measurements made at daily intervals fall within these limits. The humidity of air supplied to the chamber can be reduced if necessary by reduction of room air humidity, but 40% is regarded as being a minimum for long term rat holding rooms.

5.2.2 Distribution of TDI vapour

Using the model 7000 monitor the distribution of TDI vapour in the two inhalation chambers has been checked at two concentrations (0.02 and 0.05 ppm). Some estimations have been made at 0.15 ppm.

The first distribution study was made at a nominal concentration of 0.02 ppm. This low concentration was selected for two reasons. Firstly, maximum losses in the chamber would be expected at the lowest TDI concentration.

Secondly, the TDI monitor is used most accurately without incorporation of a dilution system and at a sensitive part of the logarithmic detection range. Samples were drawn from 26 sites within the chamber, distributed as shown in Fig.9. Sampling was limited to one half of the chamber because the chambers are symmetrical around a central axis and because, when drawing samples using the TDI monitor, losses of TDI would be expected in long sample tubes (Pratt & Edward).

Glass sample tubes of 6 mm internal diameter were used for sampling and these were connected directly to the inlet tube of the TDI monitor. Where samples were taken adjacent to a chamber wall a gap of 10 cm was allowed between the wall and the end of the sampling tube.

The total air flow rate was adjusted to 1000 l/min.

The results obtained are shown in Table 2 and represent probably the worst possible situation in the chambers.

The TDI vapour concentration was measured at 9 sites in the top part of the chamber (mean 0.022 ppm), and 8 sites half way down the chamber (0.017 ppm) and at 9 sites at the bottom of the chamber (0.011 ppm).

A good distribution was obtained at the high level as TDI entered the chamber, but in ing down the chamber some TDI was lost, probably due to the combined effects of adsorption of TDI onto cage and wall surfaces and hydrolysis in the moist air in the chamber (50% humidity).

The mean concentration at the left hand side of the chamber was 0.019 ppm, in the centre of the chamber was 0.015 ppm, and between these sites in and around the batteries was 0.017 ppm. Good distribution in the vertical plane was therefore obtained.

The second concentration used for chamber distribution studies was 0.05 ppm. Again 25 sites were analysed (Table 3). Distribution across the top plane of the chamber (mean 0.051 ppm) was not quite as good as in the earlier study, but some inaccuracies may be due to losses in the monitoring system. Half way down the chamber mean levels were 0.040 ppm and at the bottom were 0.035 ppm. Distribution in the vertical plane was again good.

It is proposed that to overcome the difficulties introduced by variation from top to bottom of the chamber, the animal cages positions will be changed on a formal schedule throughout the study.

At a nominal 0.15 ppm (0.12 ppm actual) fewer results have been obtained due to the difficulty in moving the monitor and dilution system around the chamber. TDI concentrations vary in a similar manner to those in the earlier studies, from 0.12 ppm at the top of the chamber to 0.090 ppm at the bottom (Table 4).

5.2.3 Rate of increase and clearance of TDI vapour

The model 7000 monitor was used to measure the rate of increase of TDI vapour to plateau levels and the rate of clearance of TDI from the chamber. The

curves obtained (Fig.10) will be used to assess the real daily exposure time during the study. Clearance rates will also be used to ensure that chambers are clear of TDI before opening for animal husbandry at the end of the exposure period.

The rate of clearance of TDI from the chamber was rapid. Ten minutes was sufficient time for chamber levels to fall from 0.05 ppm to 0.01 ppm . Thereafter a fall to 0.005 ppm took a further 5 minutes. Build-up of TDI within the chamber was equally rapid. A concentration of 0.15 ppm was reached from 0.00 ppm in 15 minutes.

5.2.4 Comparison of Marcali method and TDI monitor in inhalation chambers

Successive estimations of TDI levels in the inhalation chambers were made using both available methods. Comparisons were made at two concentrations and an acceptable agreement found. Results are shown in Table 5.

6. CONCLUSION

A system for long term exposure of rats to TDI vapour has been prepared and tested. The results given here demonstrate that controlled TDI concentrations can be maintained in the inhalation chambers and that monitoring systems are satisfactory.

In assessing the data provided, it must be recognised that a distribution study covering 25 sites takes three working days to complete, because of the delay inherent in the monitoring system. During this time some fluctuation in chamber atmospheres could occur, together with reduction of the yield of TDI in the monitoring system. These factors could lead to larger apparent variations between individual sites than are actually present. When the distribution study is repeated in the presence of the rats the concentration at each site will be compared to one selected site to improve the reproducibility.

The main adverse feature emerging from the results obtained to date is the loss of TDI towards the bottom of the chamber. Because of this loss, chamber atmospheres will be routinely sampled halfway down the chamber and the concentration at this point will be set to the required figure (0.05 - 0.15 ppm).

Rats will be exposed at all possible sites in the chamber, positions being changed in a formal schedule.

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TABLE 1

COMPARISON OF TWO METHODS OF ANALYSIS OF TDI VAPOUR

Analysis No.	ppm TDI	
	Marcali Method	Model 7000 Monitor
1	0.007	0.012
2	0.014	0.019
3	0.020	0.029
4	0.025	0.029
5	0.036	0.045
6	0.046	0.050

Notes

1. Monitor Serial No. 1264

2. Results obtained using the laboratory system

TABLE 2

TDI DISTRIBUTION IN EXPOSURE CHAMBERS

NOMINAL CONCENTRATION 0.02 ppm

		Concentration of TDI (ppm)		
		Left hand side	Centre of batteries	Centre of Chamber
Front plane	Top	0.026	0.028	0.023
	Centre	0.023	0.018	0.019
	Bottom	0.011	0.014	0.016
Centre plane	Top	0.024	0.018	0.021
	Centre	0.020	N/A	0.011
	Bottom	0.007	0.008	0.008
Rear Plane	Top	0.022	0.020	0.018
	Centre	0.019	0.015	0.014
	Bottom	0.011	0.014	0.009
	Mean	0.018	0.017	0.015

N/A Not accessible

Mean concentration in chamber = 0.017 ppm

Mean concentration at top level = 0.022 ppm (29% high)

Mean concentration at middle level = 0.017 ppm

Mean concentration at bottom level = 0.011 ppm (35% low)

TABLE 3

TDI DISTRIBUTION IN EXPOSURE CHAMBER

NOMINAL CONCENTRATION 0.05 ppm

		Right hand side	Centre of batteries	Centre
Front plane	Top	0.065	0.054	0.066
	Centre	0.048	0.038	0.038
	Bottom	0.029	0.032	0.033
Centre plane	Top	0.065	0.038	0.035
	Centre	0.038	0.030, 0.027	N/A
	Bottom	0.038	-	0.036
Rear plane	Top	0.042	0.045	-
	Centre	0.042	0.050	0.038
	Bottom	0.032	0.040	0.040
	Mean	0.044	0.041	0.041

N/A Not accessible

Mean concentration in chamber = 0.042 ppm

Mean concentration at top level = 0.051 ppm (28% high)

Mean concentration at centre level = 0.040 ppm

Mean concentration at bottom level = 0.035 ppm (18% low)

TABLE 4

TDI CONCENTRATIONS IN EXPOSURE CHAMBERS

NOMINAL CONCENTRATION 0.15 ppm

	TDI concentration (ppm)	
	Individual values	Mean
Top level	0.113, 0.106, 0.117, 0.148	0.12
Middle level	0.134, 0.109, 0.089, 0.095	0.11
Bottom level	0.068, 0.080, 0.100, 0.090	0.90

TABLE 5

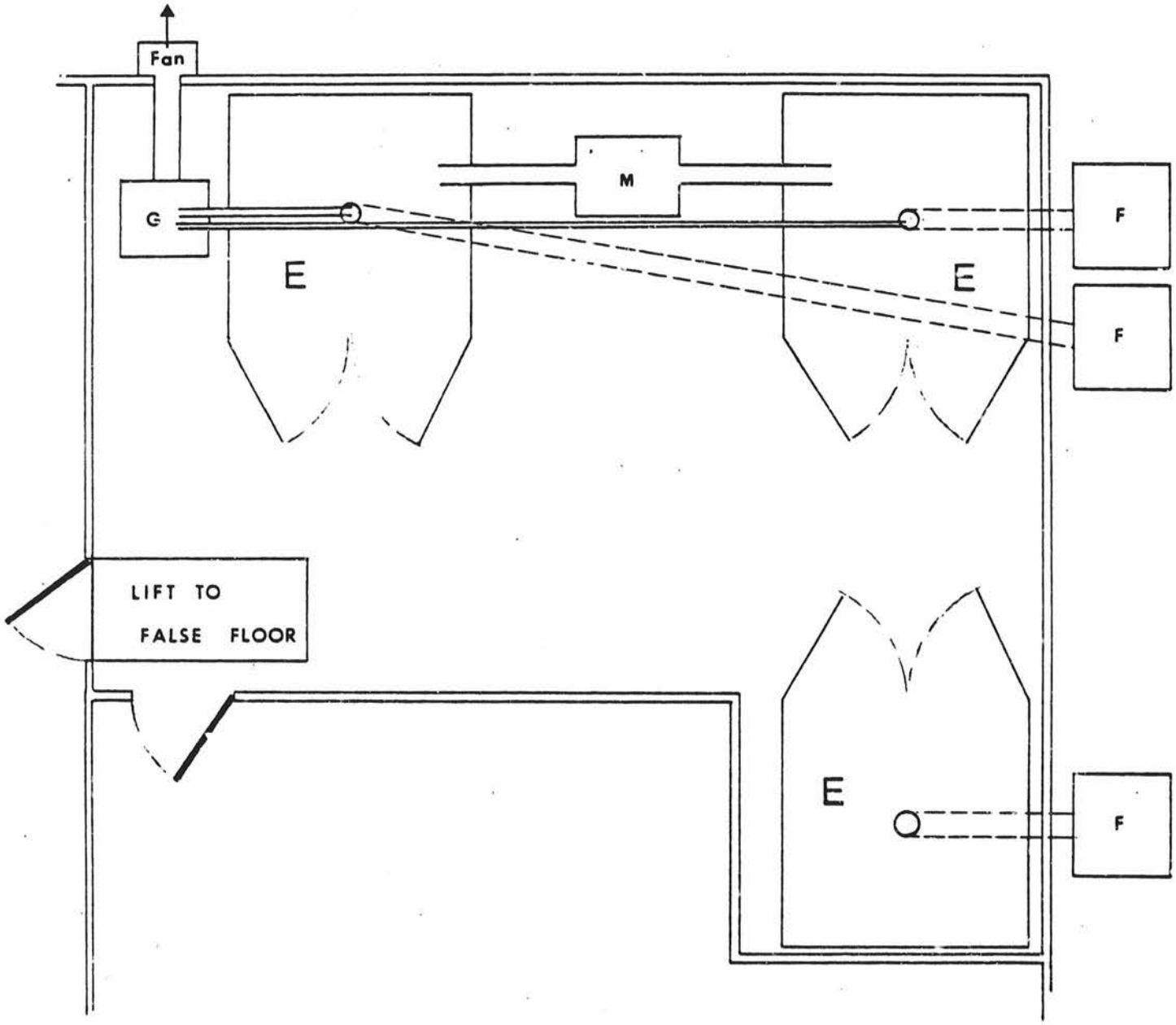
ESTIMATION OF TDI LEVELS IN INHALATION CHAMBERS USING TWO METHODS

Analysis No.	ppm TDI	
	by Model 7000 monitor	by Marcali method
1	0.030[A], 0.027[A]	0.027
2	0.038[A]	0.029
3	0.032[A]	0.023
4	0.144[B]	0.117
5	0.140[B]	0.137
6	0.134[B]	0.125
7	0.140[B]	0.129

A - without using Monitor dilution system

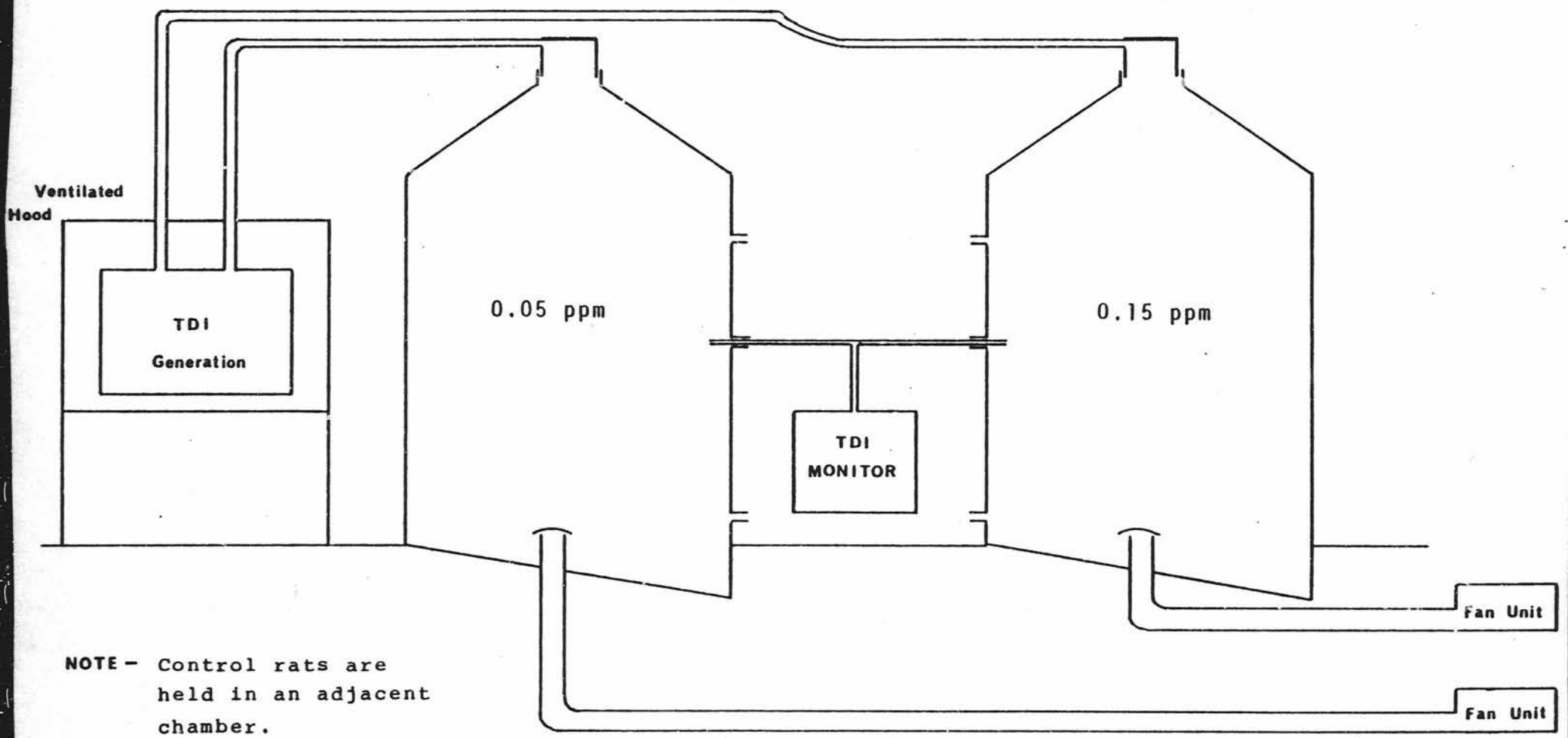
B - Using monitor dilution system

FLOOR PLAN OF ROOM PREPARED FOR RAT INHALATION STUDY.



M - MODEL 7000 TDI MONITOR
E - EXPOSURE CABINET HOLDING 2 RAT BATTERIES
G - VENTILATED CABINET FOR VAPOUR GENERATION
F - EXTRACTION FILTER AND FAN SYSTEM (OUTSIDE BUILDING

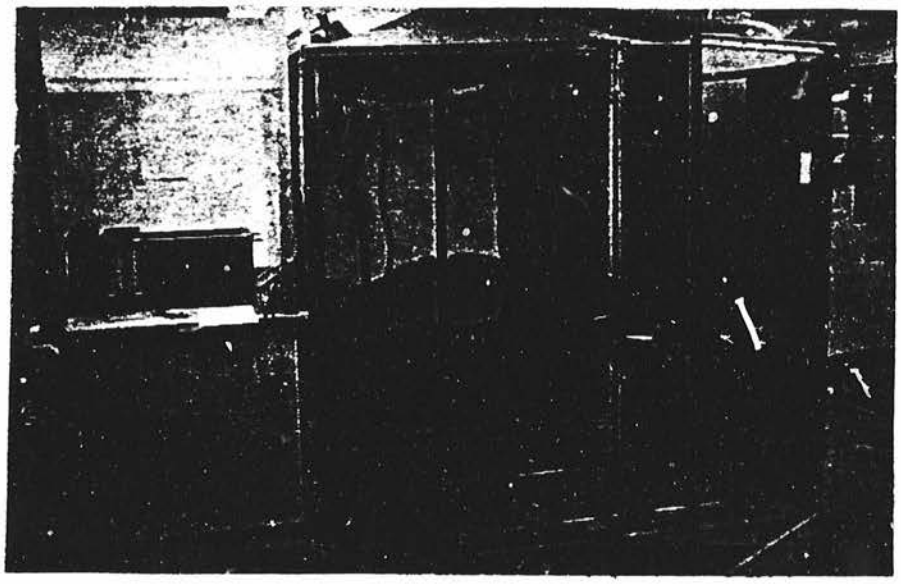
SYSTEM FOR EXPOSING RATS TO TDI VAPOUR



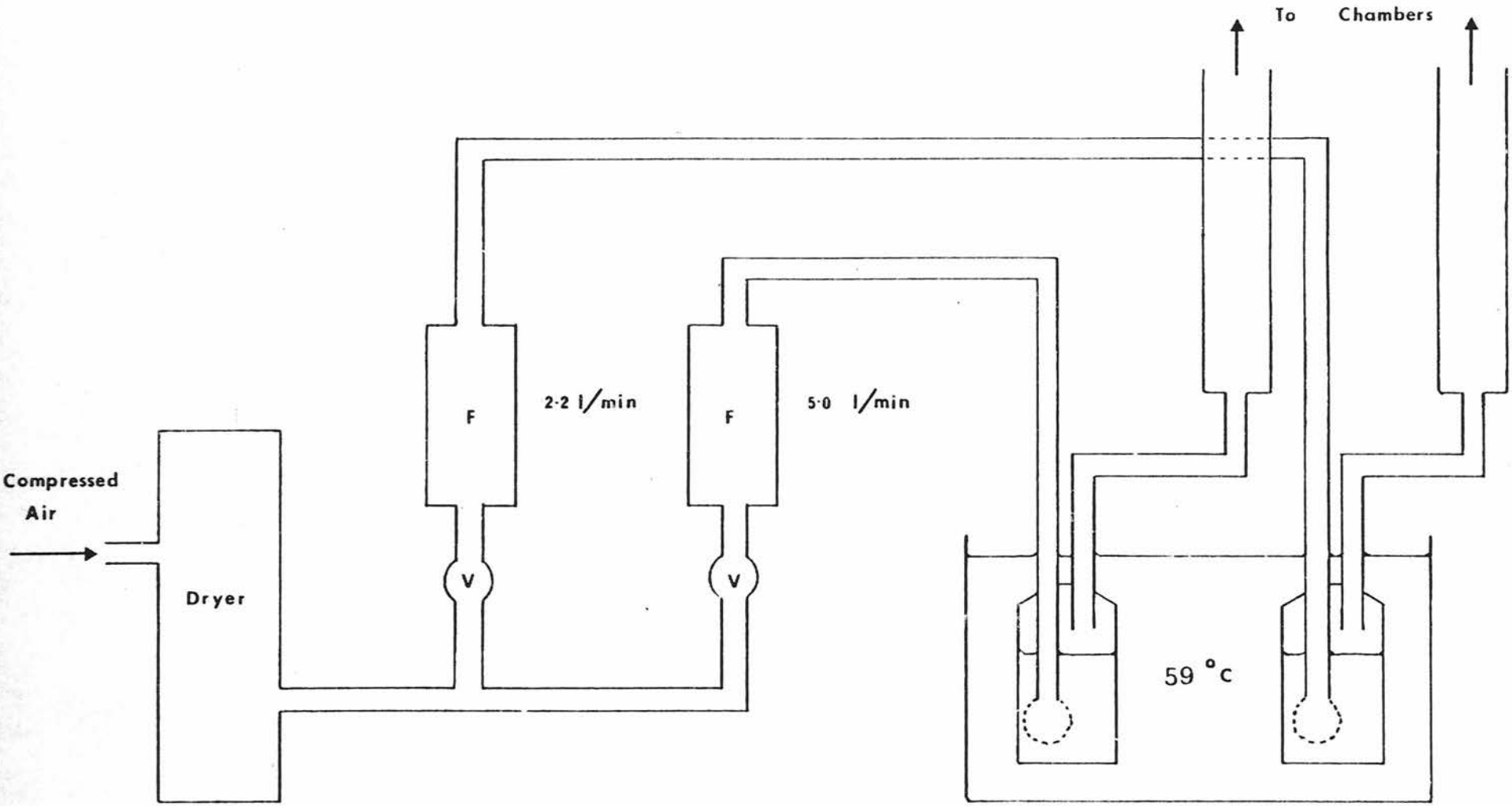
NOTE – Control rats are held in an adjacent chamber.

FIG 2A

INHALATION CHAMBER AND VAPOUR GENERATION SYSTEM



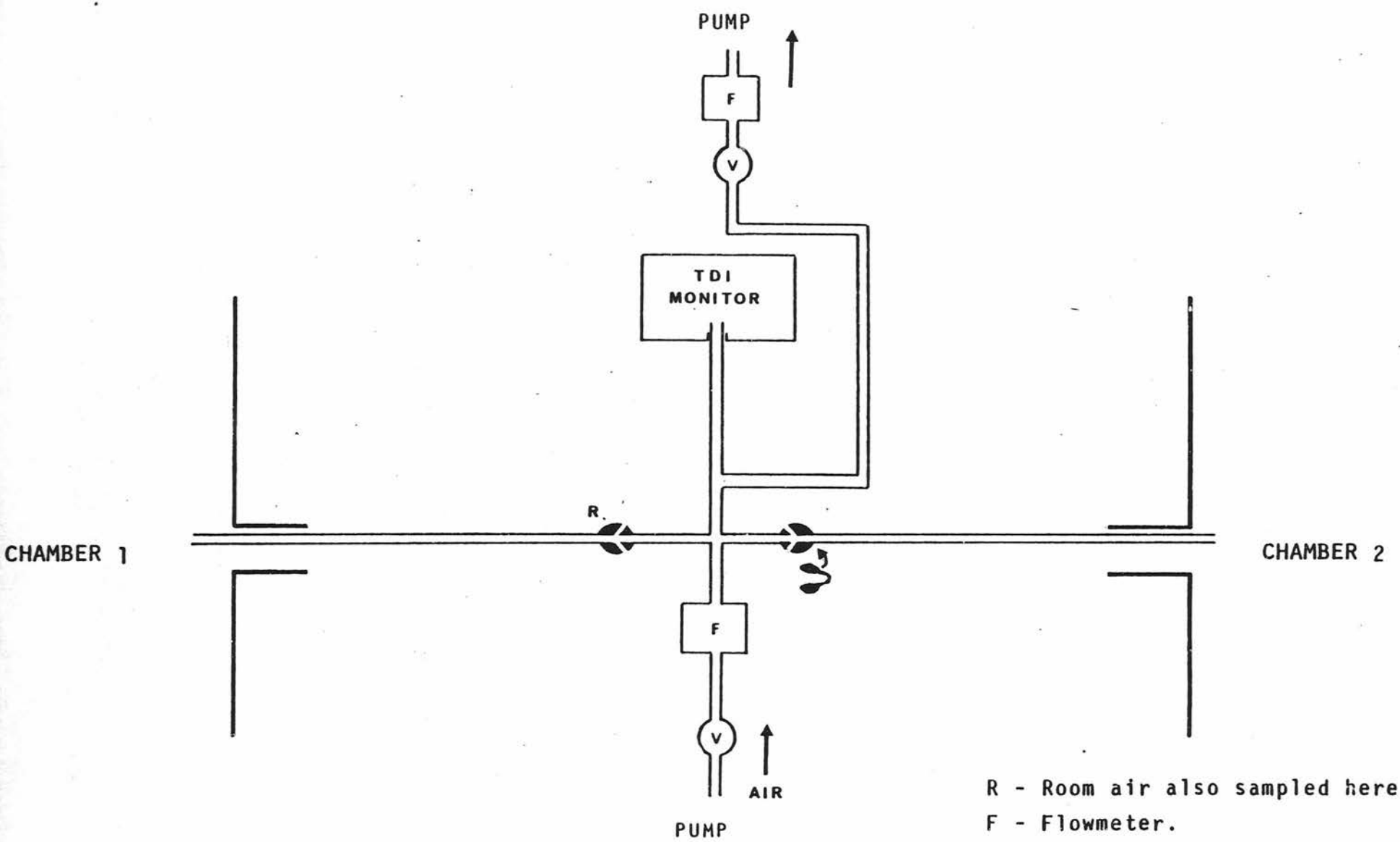
GENERATION OF TDI VAPOUR FOR INHALATION STUDIES



F - Flowmeter

V - Needlevalve

FIG. 3.



R - Room air also sampled here.
F - Flowmeter.
V - Needle valve.
C - Closing Tube to seal chamber tube not in use

FIG. 4.

MONITORING SYSTEM FOR INHALATION STUDY

Inhalation Chamber Atmosphere Control - TDI

PROJECT NUMBER	DOSE LEVEL	CHAMBER NUMBER

DATE	TIME	WATER BATH TEMP. °C	TDI FLOW RATE TO CHAMBER ml/min	DILUENT/ AIR FLOW RATE ml/min	MONITOR FLOW RATE ml/min	MONITOR READING ppm	CORRECTED CONC'N ppm	MAIN AIR FLOW RATE L/min	SIGNATURE

551/215

SYSTEM FOR COMPARISON OF TDI ANALYTICAL METHODS

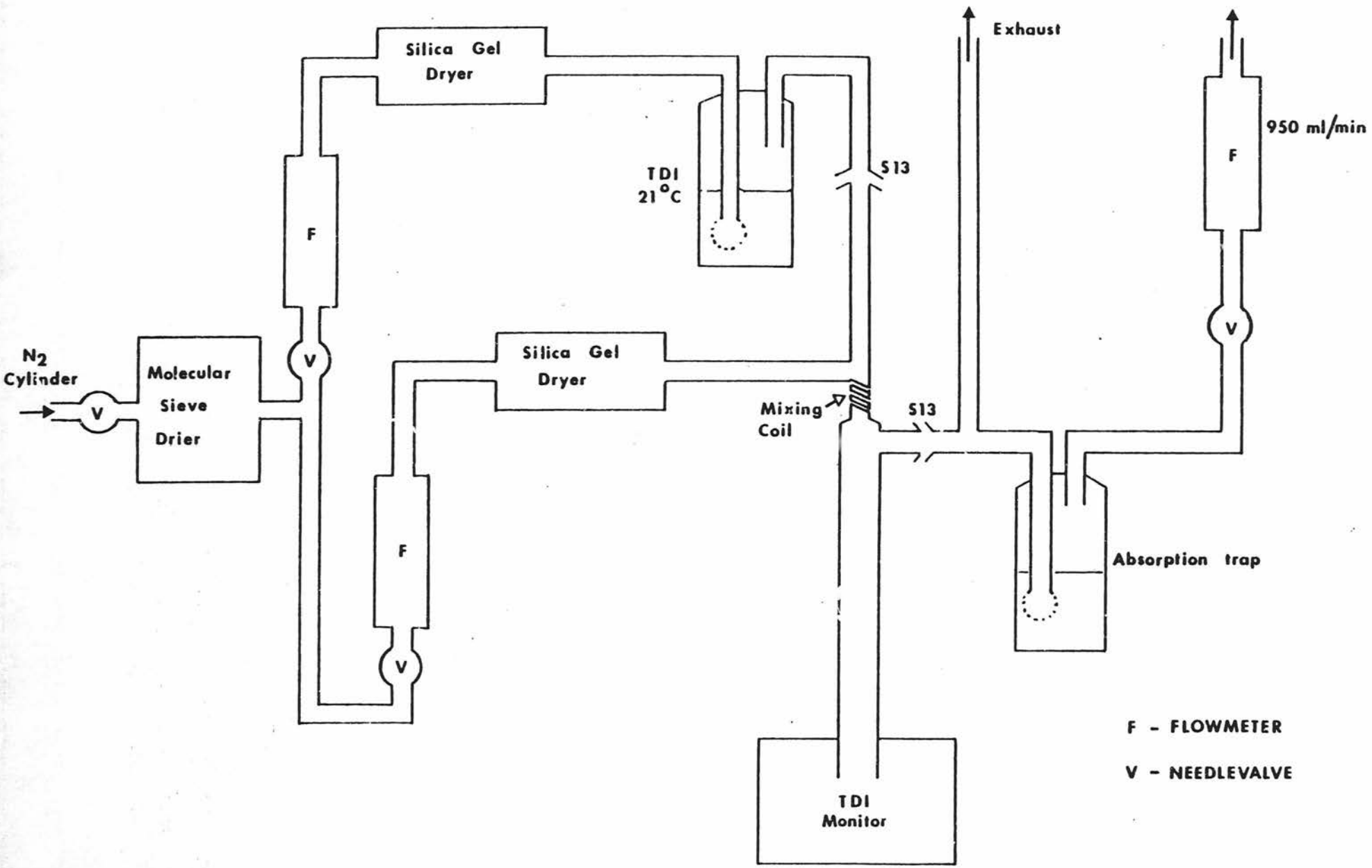
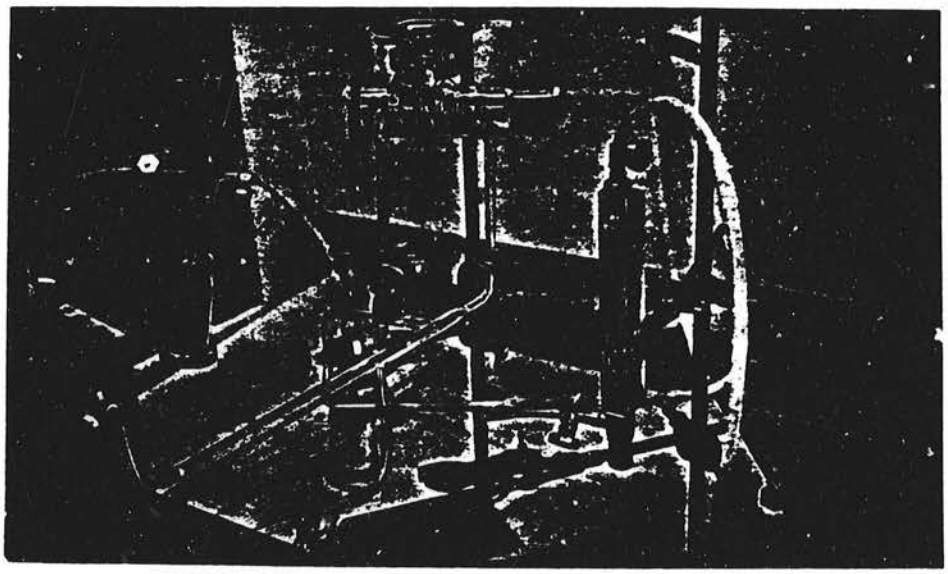


FIG. 9

FIG. 6A

LABORATORY SYSTEM FOR TDI MONITOR CALIBRATION



CALIBRATION CURVE FOR TDI ESTIMATION BY METHOD OF MARCALI (1957)

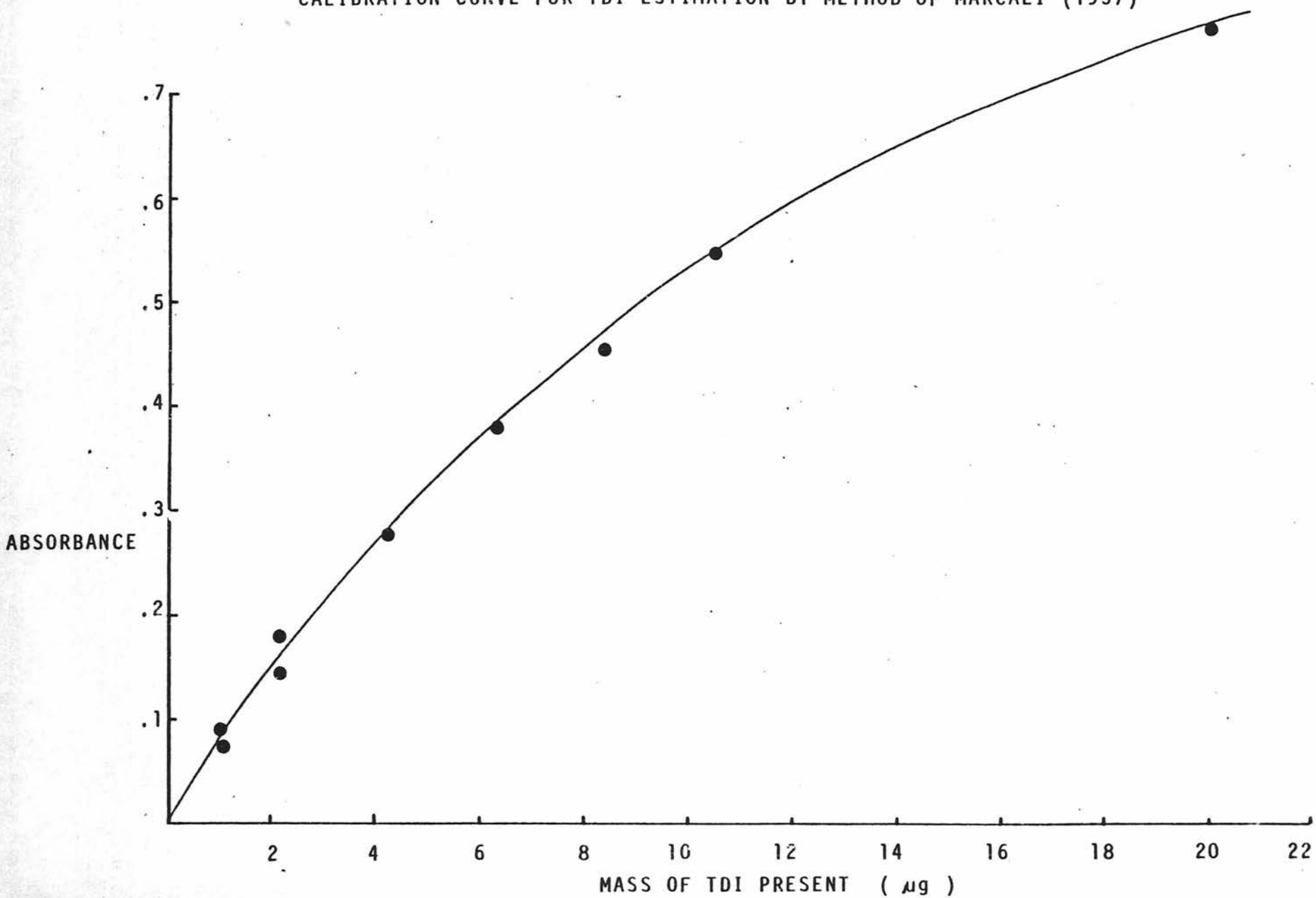
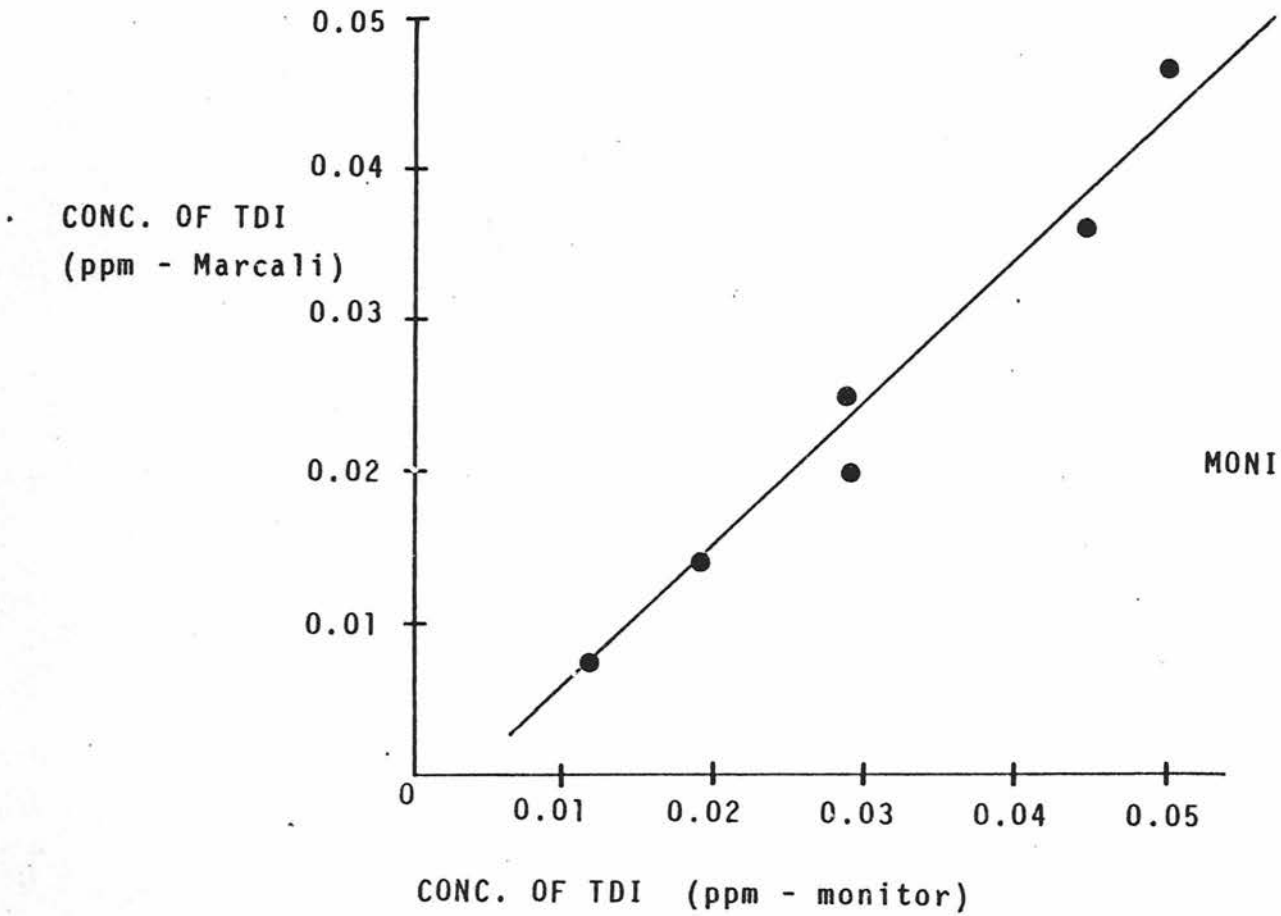


FIG. 7

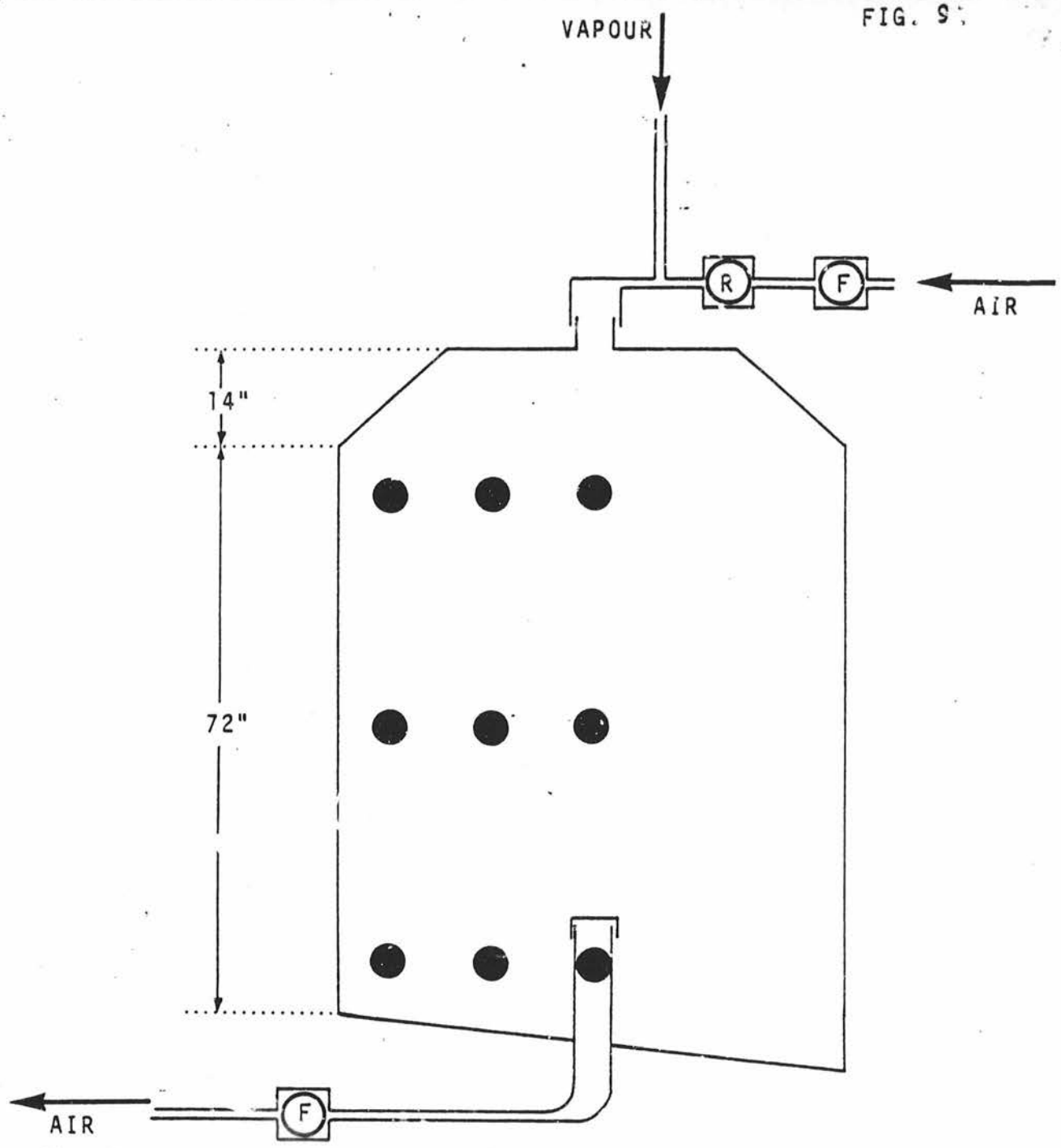
COMPARISON OF MARCALI METHOD AND MODEL 7000 MONITOR FOR TDI ANALYSIS

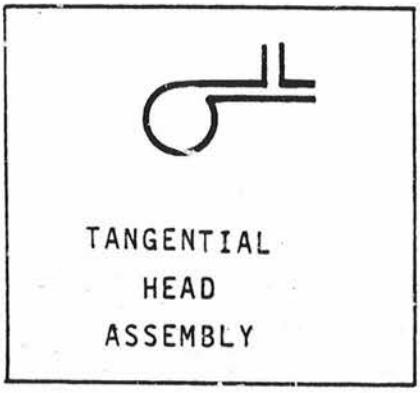


MONITOR SERIAL NUMBER 1264

FIG. 8

FIG. 9





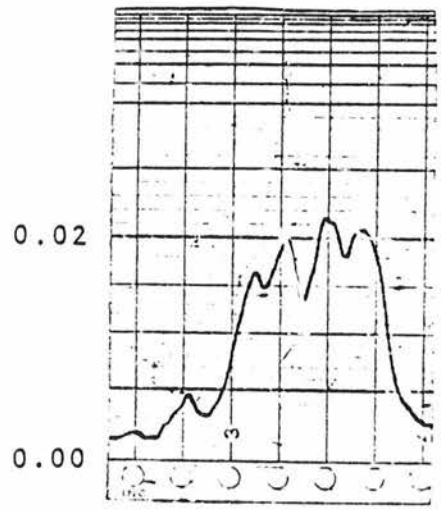
SAMPLE POINTS

R ROTAMETER

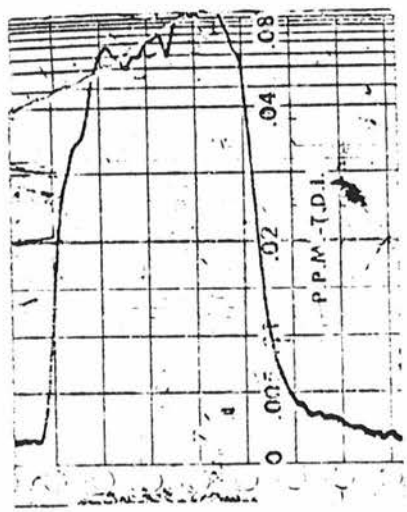
F FILTER

HLE INHALATION CHAMBER

BUILD UP AND CLEARANCE OF TDI VAPOUR IN INHALATION CHAMBERS.



BUILD UP CLEARANCE



EACH DIVISION = 15 MINUTES

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